

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

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Serial No.:)

Examiner: William Sandals

Filed:)

Group Art Unit: 1636)

For: Intravascular Delivery of Non-Viral Nucleic Acid

PRELIMINARY AMENDMENT

Commissioner of Patents
and Trademarks
Washington, D.C. 20231

Dear Sir:

This application is a divisional codepending from Serial No. 09/450,315. Kindly amend the application as follows:

In the Specification:

On page 3 line 1, please add:

Brief Description of the Drawings

- FIG. 1 illustrates high level luciferase expression in liver following tail vein injections.
- FIG. 2 indicates high level luciferase expression in spleen, lung, heart and kidney following tail vein injections.
- FIG. 3 illustrates Tail vein injection of pCILuc/polycation complexes in 2.5 ml ringers solution into 25 gram mice.

On page 11, line 7, please delete: -- **The graph above** -- and substitute -- -- **FIG. 1** -- --

On page 12, line 43, please delete: -- **The graph above** -- and substitute -- -- **FIG. 2** -- --

On page 31, line 43, please delete: -- **Tail vein injection** -- and substitute -- -- **FIG. 3 illustrates tail vein injections** -- --

In the Claims:

Please delete claims 1-15 and substitute claims 1-18 as follows:

- 1) A process for delivering a polynucleotide into an extravascular parenchymal cell of a mammal, comprising:
 - a) inserting the polynucleotide into a mammalian blood vessel, in vivo;
 - b) increasing the permeability of the blood vessel;
 - c) passing the polynucleotide through the blood vessel into the extravascular space;
 - d) delivering the polynucleotide into the mammalian extravascular parenchymal cell; and,
 - e) expressing the polynucleotide.
- 2) The process of claim 1 wherein increasing the permeability of the blood vessel consists of increasing pressure against blood vessel walls.
- 3) The process of claim 2 wherein increasing the pressure consists of increasing a volume of fluid within the blood vessel.
- 4) The process of claim 3 wherein increasing the volume consists of inserting a solution containing the polynucleotide into the blood vessel.
- 5) The process of claim 4 wherein increased pressure is controlled by altering the volume of the solution in relation to the time period of insertion.
- 6) The process of claim 5 wherein the blood vessel consists of a tail vein.
- 7) The process of claim 1 wherein the cell is selected from the group consisting of a liver cell, spleen cell, heart cell, kidney cell, prostate cell, skin cell, testis cell, skeletal muscle cell, fat cell, bladder cell, brain cell, pancreas cell, thymus cell, and lung cell.
- 8) A process for delivering a polynucleotide complexed with a compound into an extravascular parenchymal cell of a mammal, comprising:
 - a) making a polynucleotide-compound complex wherein the zeta potential of the complex is less negative than the polynucleotide alone;
 - b) adding another compound to the complex to increase zeta potential negativity of the complex from the previous step;
 - c) inserting the complex into a mammalian blood vessel;
 - d) increasing the permeability of the blood vessel;
 - e) passing the polynucleotide through the blood vessel;
 - f) delivering the polynucleotide into the mammalian extravascular parenchymal cell; and,

g) expressing the polynucleotide.

- 9) The process of claim 8 wherein increasing the permeability of the blood vessel consists of increasing pressure against blood vessel walls.
- 10) The process of claim 9 wherein increasing the pressure consists of increasing a volume of fluid within the blood vessel.
- 11) The process of claim 10 wherein increasing the volume consists of inserting a solution containing the polynucleotide into the blood vessel.
- 12) The process of claim 11 wherein a specific volume of the solution is inserted within a specific time period.
- 13) The process of claim 12 wherein increased pressure is controlled by altering the volume of the solution in relation to the time period of insertion.
- 14) The process of claim 13 wherein the blood vessel consists of a tail vein.
- 15) The process of claim 8 wherein the cell is selected from the group consisting of a liver cell, spleen cell, heart cell, kidney cell, prostate cell, skin cell, testis cell, skeletal muscle cell, fat cell, bladder cell, brain cell, pancreas cell, thymus cell, and lung cell.
- 16) The process of claims 1 and 8 wherein the polynucleotide is inserted in at least a 1 milliliter solution.
- 17) The process of claims 1 and 8 wherein the extravascular parenchymal space consists of the hepatocytes.
- 18) The process of claim 17 wherein intrahepatic parenchymal pressure is at least 10 mm mercury.

REMARKS


Amino Acid Sequence:

A Sequence Listing has been submitted with the prior application from which this divisional depends.

Drawings:

Drawings have been submitted with this Response and wording describing the figures has been added to the specification as amended above. The words have been taken directly from the specification and no new matter has been added.

Respectfully submitted,




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